

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

A Notice of Compliance with Conditions (NOC/c) is a type of approval to sell a drug in Canada.

VENCLEXTA[®] (venetoclax) used in combination with rituximab in the treatment of patients with chronic lymphocytic leukemia (CLL) who were previously treated for their cancer, has been approved without conditions.

VENCLEXTA used alone in the treatment of patients with CLL who were previously treated for their cancer has been approved *with conditions*. This means it has passed Health Canada's review and can be bought and sold in Canada, but the manufacturer has agreed to complete more studies to make sure the drug works the way it should. For more information, talk to your healthcare professional.

Health Canada only gives an NOC/c to a drug that treats, prevents, or helps identify a serious or life-threatening illness. The drug must show promising proof that it works well, is of high quality, and is reasonably safe. Also, the drug must either respond to a serious medical need in Canada, or be much safer than existing treatments.

Drug makers must agree in writing to clearly state on the label that the drug was given an NOC/c, to complete more testing to make sure the drug works the way it should, to actively monitor the drug's performance after it has been sold, and to report their findings to Health Canada.

Pr**VENCLEXTA**[®]

venetoclax tablets

Read this carefully before you start taking **VENCLEXTA** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **VENCLEXTA**.

Serious Warnings and Precautions

VENCLEXTA should only be prescribed by a doctor who is experienced in the use of anti-cancer drugs.

VENCLEXTA is only available through specialty pharmacies and/or retail oncology pharmacies that are part of AbbVie's managed distribution program.

VENCLEXTA can cause a serious side effect known as tumour lysis syndrome (TLS).

- To reduce your risk of TLS:
 - You will start taking VENCLEXTA at a low dose. Your dose will be increased weekly over 5 weeks up to the full dose.
 - Your doctor will do blood tests during the first 5 weeks to check for TLS.
 - You will need to drink plenty of water. You may need to receive intravenous fluids at an outpatient clinic or hospital on specific days during the first 5 weeks. You will also receive other medicines before starting VENCLEXTA to reduce your risk of TLS.
 - Do not take any medicines that may have a strong interaction with VENCLEXTA.

What is VENCLEXTA used for?

VENCLEXTA is used to treat patients with chronic lymphocytic leukemia (CLL) when the disease has come back or has not responded to treatment.

VENCLEXTA may be given to you alone or in combination with another medicine called rituximab.

How does VENCLEXTA work?

VENCLEXTA works by blocking a protein in the body called "BCL-2". This is a protein that helps cancer cells survive. Blocking this protein helps to kill and lower the number of cancer cells.

What are the ingredients in VENCLEXTA?

Medicinal ingredient: venetoclax

Non-medicinal ingredients: calcium phosphate dibasic, colloidal silicon dioxide, copovidone, iron oxide yellow, polyethylene glycol, polysorbate 80, polyvinyl alcohol, sodium stearyl fumarate, talc and titanium oxide

The 50 mg tablet also contains iron oxide black and iron oxide red.

VENCLEXTA comes in the following dosage forms:

Tablets: 10 mg, 50 mg and 100 mg

Do not use VENCLEXTA if:

- You are allergic to any of the ingredients.
- You are taking certain medicines when you start your treatment and during the time when your dose is gradually being increased (usually over 5 weeks) because they may have a strong interaction with VENCLEXTA. Some of these medicines include:
 - itraconazole, ketoconazole, posaconazole or voriconazole for fungal infections
 - clarithromycin for bacterial infections
 - ritonavir for HIV infection

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take VENCLEXTA. Talk about any health conditions or problems you may have, including if you:

- have kidney or liver problems
- have any signs or symptoms of infection such as fever, chills, cough, feeling weak or confused, or a painful or burning feeling when passing urine
- have recently received or are scheduled to receive a vaccine

Other warnings you should know about:

Other cancers:

During treatment with VENCLEXTA, a higher number of cases of certain types of non-melanoma skin cancer have been reported. Your healthcare professional will monitor you for the signs of skin cancer.

Tumour Lysis Syndrome

VENCLEXTA can cause a serious side effect called tumour lysis syndrome (TLS). TLS is caused by the fast breakdown of cancer cells. As cancer cells are destroyed, they release their contents, leading to high levels of certain chemicals (potassium, uric acid, phosphorus) and low

levels of calcium in the blood. High, or low, levels of these chemicals can cause serious damage to your kidneys, or other organs, and may lead to death. TLS is most likely to occur in the first 5 weeks of treatment. The changes in your blood that could lead to TLS may have no symptoms. Having your blood tested is important in order to treat and prevent TLS. The symptoms below can be associated with rapid cell death or TLS:

- fever
- chills
- nausea (feeling sick to your stomach)
- vomiting
- confusion
- shortness of breath
- seizure
- irregular heartbeat
- dark or cloudy urine
- unusual tiredness
- muscle pain
- joint discomfort

If you notice any of these, call your doctor or nurse right away.

- Your doctor will do tests to check your risk of getting TLS before you start taking VENCLEXTA. Your doctor will also do blood tests during your first 5 weeks of treatment to check for TLS. It is important to keep your scheduled appointments for blood tests.
- Your doctor will give you other medicines before starting and during treatment with VENCLEXTA to help reduce your risk of TLS.
- You will need to drink plenty of water when taking VENCLEXTA to help reduce your risk of getting TLS. Follow the instructions about drinking water in the Quick Start Guide and as labelled inside the weekly wallet blister packs.
- Your doctor may hospitalize you before you start VENCLEXTA to give intravenous (IV) fluids into your vein, do blood tests, and check for TLS.

Adults 65 years of age and older:

Adults 65 years of age and older may be more likely to experience certain side effects when taking VENCLEXTA in combination with rituximab.

Children and adolescents less than 18 years of age:

It is not known if VENCLEXTA is safe or will work in children or adolescents less than 18 years of age.

Pregnancy, breastfeeding, contraception and fertility:

- VENCLEXTA should not be used during pregnancy. It may harm your unborn baby. Tell your doctor immediately if you become pregnant.
- Women who are able to become pregnant should have a pregnancy test before starting treatment with VENCLEXTA and should use effective birth control (contraception) during treatment with VENCLEXTA and for at least 30 days after stopping treatment.
- Do not breastfeed while you are taking this medicine.
- VENCLEXTA may cause male infertility (low or no sperm count). This may affect your ability to father a child. Ask your doctor for advice before starting treatment with VENCLEXTA.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following list contains examples of food or drugs that may interact with VENCLEXTA:

- some medicines used to treat fungal infections – like fluconazole, itraconazole, ketoconazole, posaconazole and voriconazole
- some medicines used to treat bacterial infections – like azithromycin, ciprofloxacin, clarithromycin, erythromycin, nafcillin and rifampin
- some medicines used to prevent seizures or to treat epilepsy – like carbamazepine and phenytoin
- some medicines used to treat HIV infection – like efavirenz, etravirine, and ritonavir
- some medicines used to treat high blood pressure or heart-related chest pain (angina) – like bosentan, captopril, carvedilol, diltiazem, felodipine, ranolazine and verapamil
- a medicine used to treat a sleep disorder (narcolepsy) known as modafinil

- some herbal medicines – like St John’s wort and quercetin
- a blood thinner known as warfarin
- some medicines used to treat heart conditions – like amiodarone, digoxin, quinidine and ticagrelor
- an immunosuppressant drug known as cyclosporine
- DO NOT eat grapefruit (or drink its juice), Seville oranges (or marmalades) or starfruit while you are taking VENCLEXTA. These products may increase the amount of VENCLEXTA in your blood.

How to take VENCLEXTA:

- Always take VENCLEXTA exactly as your doctor tells you.
- Drink plenty of water when taking VENCLEXTA to help reduce your risk of getting TLS.
- Take the tablets with a meal and water at the same time each day.
- Swallow VENCLEXTA tablets whole. Do not chew, crush, or break the tablets.

When starting VENCLEXTA:

- Read the Quick Start Guide that comes with your Starting Pack (which contains 4 weekly wallet blister packs).
- Drink 7 glasses of water each day (1.75 litres total). Start drinking this amount of water 2 days before your first dose. Continue to drink this amount each day. This is especially important on the 2 days leading up to your first dose and every time your dose is increased (days 1, 6 and 7 of each week). Follow the instructions about drinking water in the Quick Start Guide and as labelled inside the weekly wallet blister packs.
- Your doctor will do required blood testing prior to starting each week of the Starting Pack, as well as 6 to 8 hours and 24 hours after your first dose for each of the first 2 weeks of VENCLEXTA treatment. Do not take your next dose until your doctor knows the results of these blood tests and tells you it is safe to do so.
- Do not start a new dose unless your doctor tells you it is safe to do so.

Usual dose:

Your doctor will start VENCLEXTA at a low dose for 1 week. Your doctor will gradually increase the dose over the next 4 weeks to the full standard dose.

The usual dose is as follows:

- The starting dose is 20 mg (two 10 mg tablets) once a day for 7 days.
- The dose will be increased to 50 mg (one 50 mg tablet) once a day for 7 days.
- The dose will be increased to 100 mg (one 100 mg tablet) once a day for 7 days.
- The dose will be increased to 200 mg (two 100 mg tablets) once a day for 7 days.
- The dose will be increased to 400 mg (four 100 mg tablets) once a day.
 - If you are taking VENCLEXTA alone, you will stay on the 400 mg daily dose, which is the standard dose, for as long as necessary.
 - If you are taking VENCLEXTA in combination with rituximab:
 - You will start your rituximab after the first five weeks of VENCLEXTA.
 - You will receive VENCLEXTA for two years.

Overdose:

If you think you have taken too much VENCLEXTA, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed dose:

- If it has been less than 8 hours, take your dose as soon as possible.
- If it has been more than 8 hours, skip the missed dose and take the next dose at your usual time the next day.
- If you vomit after taking VENCLEXTA, do not take an extra dose. Take the next dose at your usual time the next day.
- If you are not sure, talk to your healthcare professional.

What are possible side effects from using VENCLEXTA?

These are not all the possible side effects you may feel when taking VENCLEXTA. If you experience any side effects not listed here, contact your healthcare professional.

Side effects may include:

- diarrhea or constipation

- nausea
- vomiting
- fever
- headache
- dizziness
- feeling tired
- cough
- muscle and joint pain
- itching

VENCLEXTA may cause abnormal blood test results. Your doctor will decide when to perform blood tests and will interpret the results.

Serious side effects and what to do about them		
Symptom/effect	Talk to your healthcare professional	Stop taking drug and get immediate medical help
VERY COMMON		
Neutropenia (low levels of white blood cells): chills, fever, sweating or any signs of infection	✓	
Anemia (low levels of red blood cells): fatigue, pale skin, shortness of breath, weakness	✓	
Thrombocytopenia (low levels of blood platelets): increases risk of bleeding or bruising	✓	
COMMON		
Pneumonia (infection of the lungs): chills, cough with or without mucus, fever, shortness of breath	✓	

Serious side effects and what to do about them		
Symptom/effect	Talk to your healthcare professional	Stop taking drug and get immediate medical help
Respiratory tract infection: runny nose, sore throat or cough	✓	
Urinary tract infection: burning sensation during urination, low urine output despite feeling urge to urinate more often	✓	
RARE		
Tumour lysis syndrome (TLS): chills, confusion, dark or cloudy urine, fever, irregular heartbeat, joint discomfort, muscle pain, nausea, shortness of breath, seizure, tiredness, vomiting		✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

<p>Reporting Side Effects</p> <p>You can report any suspected side effects associated with the use of health products to Health Canada by:</p> <ul style="list-style-type: none"> • Visiting the Web page on Adverse Reaction Reporting (www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting) for information on how to report online, by mail or by fax; or • Calling toll-free at 1-866-234-2345. <p><i>NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.</i></p>

Storage:

Store between 2 and 30°C.

Keep out of reach and sight of children.

Access to VENCLEXTA

VENCLEXTA is only available through specialty pharmacies and/or retail oncology pharmacies that are part of AbbVie's managed distribution program. Talk to your doctor for more information.

If you want more information about VENCLEXTA:

- Talk to your healthcare professional.
- Find the most recent version of the full Product Monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the [Health Canada website](http://www.canada.ca/en/health-canada) (www.canada.ca/en/health-canada), the manufacturer's website (abbvie.ca), or by calling 1-888-704-8271.

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